CLAIMS

What is Claimed is:

1. A thioester or selenoester generator comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone having side chains lacking reactive functional groups, said N-terminal group comprising a first amino acid residue having a backbone nitrogen anchored to a support through a nucleophile-stable linker, and said C-terminal group comprising a second amino acid residue having a backbone carbonyl of an ester, wherein said first and second amino acid residues are separated by one or more additional amino acid residues.

2. The thioester or selenoester generator according to Claim 1, wherein said backbone nitrogen is protected with an amino protecting group.

3. The thioester or selenoester generator according to Claim 1, wherein said backbone nitrogen is coupled to an additional amino acid or peptide.

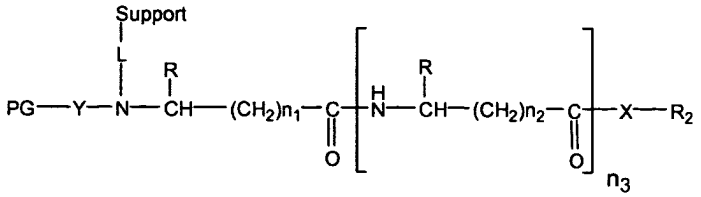
4. The thioester or selenoester generator according to Claim 3, wherein said additional amino acid or peptide is capable of supporting chemical ligation.

5. The thioester or selenoester generator according to Claim 4, wherein said additional amino acid or peptide comprises a side chain group.

6. The thioester or selenoester generator according to Claim 4, wherein said additional amino acid or peptide comprises a terminal group.

7. The thioester or selenoester generator according to Claim 1, wherein said ester is a member selected from the group consisting of a thioester and a selenoester.

8. A thioester or selenoester generator comprising the formula:



wherein:

Y is a target molecule of interest that may be present or absent, and is lacking reactive functional groups;

PG is a protecting group that may be present or absent, and is an amino protecting group when Y is absent;

L is a nucleophile-stable linker;

Support is chosen from a solid phase, matrix, or surface;

R is hydrogen or any organic side chain lacking reactive functional groups;

$n_1$and n_2 each are from 0 to 2;

n_3 is from 2 to 20;

X is oxygen, sulfur, or selenium;

R_2 is a protecting group removable under conditions orthogonal to PG when X is oxygen; and

R_2 is any group compatible with thioesters or selenoesters when X is sulfur or selenium.

9. A method of generating a thioester or selenoester, said method comprising:

(a) providing a composition comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone lacking reactive functional groups, said N-terminal group comprising a first amino acid residue having a backbone nitrogen anchored to a support through a nucleophile-stable linker, and said C-terminal group comprising a second amino acid residue having a backbone carboxyl protected with a carboxyl protecting group removable under conditions orthogonal to said nucleophile-stable linker, wherein said first and second amino acid residues are separated by one or more additional amino acid residues;

(b) forming an elongated product having one or more additional amino acids or peptides that extend from, and is covalently joined to, said backbone nitrogen, with the proviso that said elongated product is lacking reactive functional groups;

(c) selectively removing said carboxyl protecting group from the product of step (b) to generate a free carboxylate; and

(d) converting said free carboxylate to a thioester or selenoester to generate said thioester or selenoester.

10. The method according to Claim 9, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

11. A method of producing a thioester or selenoester generator, said method comprising:

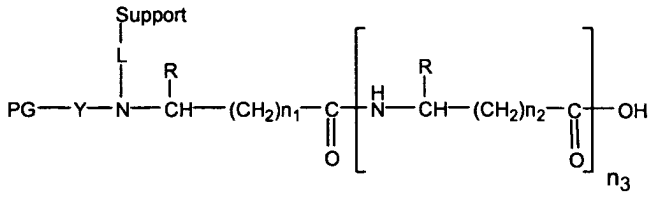
(a) providing a composition comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone having side chains lacking reactive functional groups, said N-terminal group comprising a first amino acid residue having a backbone nitrogen anchored to a support through a nucleophile-stable linker and lacking reactive functional groups, and said C-terminal group comprising a second amino acid residue having a free backbone carboxyl, wherein said first and second amino acid residues are separated by one or more additional amino acid residues; and

(b) converting said backbone carboxyl to a thioester or selenoester.

12. The method according to Claim 11, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

13. A method of producing a thioester or selenoester generator, comprising:

(a) providing a precursor compound having the formula:



wherein:

Y is a target molecule of interest that may be present or absent, and is lacking reactive functional groups;

PG is a protecting group that may be present or absent, and is an amino protecting group when Y is absent;

L is a nucleophile-stable linker;

Support is chosen from a solid phase, matrix, or surface;

R is hydrogen or any organic side chain lacking reactive functional groups;

n_1 and n_2 each are from 0 to 2; and

n_3 is from 2 to 20; and

(b) converting said C-terminal carboxyl of said precursor compound to a thioester or selenoester.

14. The method according to Claim 13, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

15. A method of generating a thioester or selenoester, comprising:

(a) providing a composition comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone lacking reactive functional groups, said N-terminal group comprising an unprotected backbone nitrogen anchored to a support through a nucleophile-stable linker, and said C-terminal group comprising a backbone carboxyl protected with a carboxyl protecting group that is removable under conditions orthogonal to said nucleophile-stable linker;

(b) coupling a peptide to said unprotected backbone nitrogen, said peptide having a C-terminal group comprising an activated carboxyester and an N-terminal group comprising an amino group protected with an amino protecting group removable under conditions orthogonal to said carboxyl protecting group;

(c) optionally, selectively removing said amino protecting group from the product of step (b) to generate an unprotected amino group, and producing an elongated product having one or more amino acids or peptides that extend from, and are covalently joined to said unprotected amino group, with the proviso that said elongated product is lacking reactive functional groups;

(d) selectively removing said carboxyl protecting group from the product of step (b) or (c) to generate a free carboxyl group; and

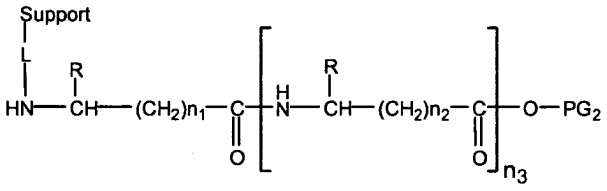
(e) converting said free carboxyl group to a thioester or selenoester to produce said thioester or selenoester.

16. The method according to Claim 15, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

17. A method of generating a thioester or selenoester, said method comprising:

(a) providing:

(i) a precursor compound having the formula:



wherein:

L is a nucleophile-stable linker;

Support is chosen from a solid phase, matrix, or surface;

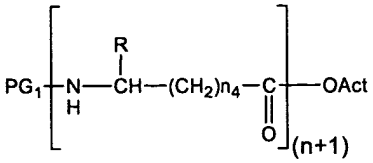
R is hydrogen or any organic side chain lacking reactive functional groups;

n_1 and n_2 each are from 0 to 2;

n_3 is from 0 to 20; and

PG_2 is a carboxyl protecting group that is removable under conditions orthogonal to L; and

(ii) a peptide of the formula:



wherein:

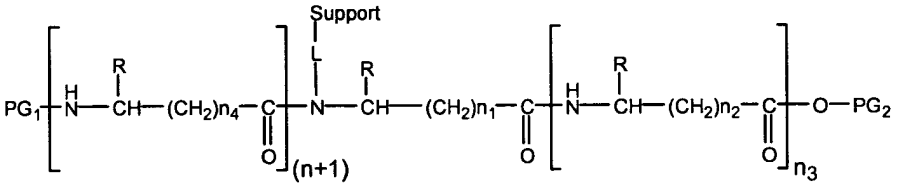
PG_1 is an amino protecting group removable under conditions orthogonal to PG_2;

n4 is 0 to 2;

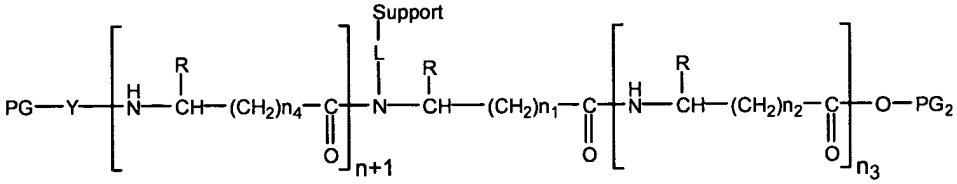
n is 1 to 20; and

OAct is an activated ester;

(b) coupling said peptide of step (a)(ii) to the unprotected amino group of the precursor compound of step (a)(i) to generate a composition having the formula:



(c) optionally, selectively removing said amino protecting group PG_1 from the product of step (b) and forming an elongated product having the formula:



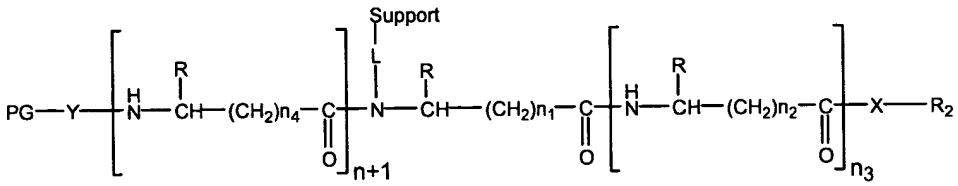
wherein:

Y is a target molecule of interest and is lacking reactive functional groups; and

PG is a protecting group that may be present or absent and is removable under conditions orthogonal to said carboxyl protecting group PG_2;

(d) selectively removing said carboxyl protecting group from the product of step (b) or (c) to generate a free carboxyl, and converting said free carboxyl to a

thioester or selenoester to generate a thioester or selenoester generator of the formula:



wherein:

PG and Y may be individually present or absent;

X is sulfur or selenium; and

R_2 is any group compatible with thioesters or selenoesters.

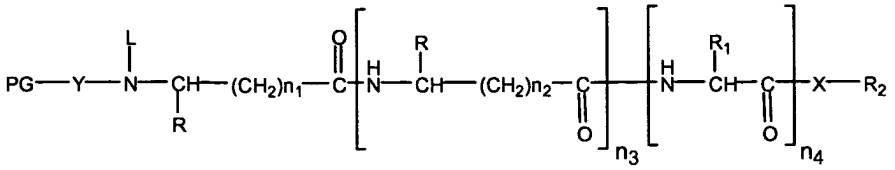
18. The method according to Claim 17, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

19. A sterically hindered thioester or selenoester generator comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone, said N terminal group comprising a backbone nitrogen anchored to a support through a nucleophile-stable linker, and said C-terminal group comprising a moiety chosen from a sterically hindered thioester or selenoester.

20. The sterically hindered thioester or selenoester generator according to Claim 19, wherein said amino acid synthon comprises two or more amino acid residues.

21. The sterically hindered thioester or selenoester generator according to Claim 19, wherein said C-terminal group comprises a backbone carbonyl.

22. A sterically hindered thioester or selenoester generator comprising the formula:



wherein:

Y is a target molecule of interest that may be present or absent, and is lacking reactive functional groups;

PG is a protecting group that may be present or absent, and is an amino protecting group when Y is absent;

L is a nucleophile-stable linker; each R and R_1 individually is hydrogen or any organic side chain group and may be the same or different;

n_1 and n_2 each individually are 0, 1 or 2;

n_3 is 0 to 20;

n_4 is 0 or 1;

X is sulfur or selenium;

R_2 is any group compatible with a thioester or selenoester; and

at least one of R, R_1 and R_2 is a group that sterically hinders the thioester or selenoester moiety –C(O)-X-.

23. A method of producing a sterically hindered thioester or selenoester generator, said method comprising:

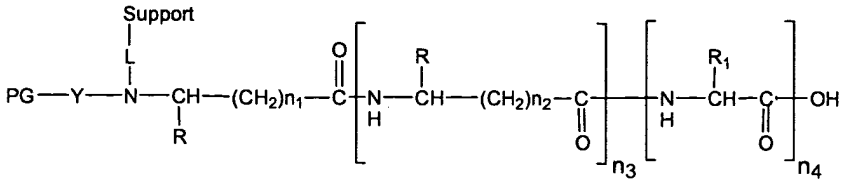
(a) providing a precursor composition comprising an amino acid synthon having an N-terminal group joined to a C-terminal group through an organic backbone lacking reactive functional groups, said N-terminal group comprising a nitrogen anchored to a support through a nucleophile-stable linker, and said C-terminal group comprising a free carboxyl; and

(b) converting said free carboxyl of said precursor composition to a sterically hindered thioester or selenoester.

24. The method according to Claim 23, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.

25. A method of producing a sterically hindered thioester or selenoester generator, said method comprising:

(a) providing a precursor composition having the formula:



wherein:

Y is a target molecule of interest that may be present or absent, and is lacking reactive functional groups;

PG is a protecting group that may be present or absent, and is an amino protecting group when Y is absent;

Support is chosen from a solid phase, matrix, or surface;

L is a nucleophile-stable linker;

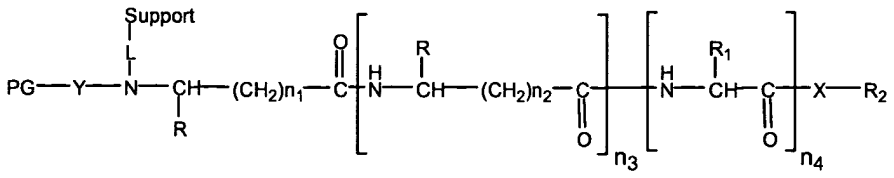
each R and R_1 individually is hydrogen or any organic side chain group and may be the same or different;

n_1 and n_2 each individually are 0, 1 or 2;

n_3 is 0 to 20; and

n_4 is 0 or 1; and

(b) converting the free carboxyl of the precursor composition step (a) to a sterically hindered thioester or selenoester to produce a sterically hindered thioester or selenoester having the formula:



wherein:

X is sulfur or selenium;

R_2 is any thioester or selenoester compatible group; and

at least one of R, R_1 and R_2 is a group that sterically hinders the thioester or selenoester moiety –C(O)-X-.

26. The method according to Claim 25, further comprising cleaving said nucleophile-stable linker under non-nucleophilic conditions.